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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/692,643	10/24/2003	Jaime L. Masferrer	3167/12A/US(6794F-000032/	8629

47376 7590 03/22/2005

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EXAMINER	
COOK, REBECCA	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 03/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/692,643	MASFERRER, JAIME L.	
	Examiner	Art Unit	
	Rebecca Cook	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *5-7,10,14-16 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8,9,11-13,17-19 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/14/03, 3/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restrictions

Applicant's election of the COX-2 inhibitor species celecoxib in the reply filed on Jnauary 4, 2005 is acknowledged. Claims 1-4, 8-9, 11-13, 17-19 and 23 read on the elected species and will be examined. Claims 5-7, 10, 14-16, 20-22 are withdrawn as not reading on the elected species.

Priority

Support for edotecarin is seen in parent 09/843,132 on page 56 (J 107088) filed April 25, 2001. However, no support is seen for said compound in parent 09/270,951 filed December 22, 1999. Support is seen for COX-2 inhibitors, including celecoxib, in 60/113,786 filed December 23, 1998.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

Claims 1-4, 8-9, 11-13, 17-19 and 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of a neoplasia does not reasonably provide enablement for prevention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.
Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have

required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,
2) the amount of direction or guidance provided,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the relative skill of those in the art,
7) the predictability of the art, and
8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to prevention of any and all neoplasias, and the relative skill of those in the art is high, generally that of a PHD or MD. This unpredictability has a number of facets, as discussed hereinafter. Additionally, the

A. Treatment by Cancer Type

While the state of the art is relatively high with regard to the prevention of specific neoplasias with specific agents, it has long been underdeveloped with regard to the prevention of neoplasias broadly. In particular, there is no known agent which is effective to prevent all neoplasias. This is why the National Cancer Institute (NCI) has the extensive *in vitro* drug screening program it does. As discussed by the court in In re Brana, 51 F.3d 1560 (Fed. Cir. 1995), *in vitro* assays are used by NCI (such as the P388 and L1210 lymphocytic leukemia tests at issue therein) to measure the potential

antitumor properties of a candidate compound. Brana at 1562-63. If success is shown in this initial screening step, this demonstrates that at least one cancer type (e.g., lymphocytic leukemia) is sensitive thereto, and provides the incentive to select it for further studies to determine its usefulness as a chemotherapeutic agent against other cancer types (lung, breast, colon, etc.) *Id.* at 1567-68. These *in vitro* tests are considered reasonably correlative of success *in vivo*.

Thus, a considerable amount of *in vitro* empirical testing is required, with no *a priori* expectation of success being present, before a candidate anticancer agent can be considered useful to prevent any and all neoplasias.

B. Combination Chemotherapy

Furthermore, the unpredictability observed with single agents is compounded when a combination of agents is used. This is summarized by WO 00/61142, at page 1, lines 17-23:

> Combination therapies, while desirable, are a hit or miss proposition. The treatments are typically not additive. In many cases, cross effects and treatment load can result in lower effectiveness for the combinations, than either treatment alone.

This is verified by U.S. Pat. 6,465,448 at col. 1, lines 56-59:

> The design of drug combinations for the chemotherapeutic treatment of cancer should be approached with the goals of 1) finding a combination that is synergistic with and not merely additive to the first compound with respect to the elimination of the tumor, and 2) finding a second drug that does not potentiate the toxic effects of the first therapeutic agent. *These conditions require a great deal of empirical testing* of agents known to have anticancer properties with agents that either may have anticancer properties, or that may augment the first agent in other ways. (Emphasis added).

Thus, when two (or more) agents are used, even more additional empirical

testing is required, again with no *a priori* expectation of success.

2. The breadth of the claims

The claims are very broad and inclusive of prevention of all "neoplasias" generally. The term "prevention' can be construed broadly as either prevention the onset of clinically evident neoplasia altogether or preventing the onset of a preclinically evident stage of neoplasia in individuals at risk. In other words, the instant claims are drawn to a composition and method of preventing all preclinical stages of any and all stages of neoplasias, which includes any undetectable stages of neoplasia.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction for ascertaining, *a priori*, which neoplasias will be prevented. It is known in the art that various factors are involved in causing various neoplasias, including genetics and environmental factors, such as diet and exposure to carcinogens.

4. The quantity of experimentation necessary

The lack of adequate guidance from the specification or prior art with regard to the actual prevention of all neoplasias in a mammal with the claimed compounds fails to rebut the presumption of unpredictability extant in this art. Applicants fail to provide the guidance and information required to ascertain which particular neoplasias the claimed agents will be effective against without resorting to undue experimentation. Applicant's disclosure of the role of celecoxib and edotecarin is noted, but is not sufficient to claiming prevention of all neoplasias broadly or even and and all malignant tumors.

Absent a reasonable *a priori* expectation of success for using a specific combination to treat any particular type of neoplasia, one skilled in the art would have to extensively test many various tumor types. Since each prospective embodiment, and indeed future embodiments as the art progresses, would have to be empirically tested, and those which initially failed tested further, an undue amount of experimentation would be required to practice the invention as its is claimed in its current scope, because the specification provides inadequate guidance to do otherwise.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 8-9, 11-13, 17-19 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over MEDLINE AN 2000061195 and WO 95/15316.

MEDLINE AN 2000061195 discloses celecoxib (page 38, line 37) and that it can be used to treat cancer (page 7, lines 27, 31). The claims differ over MEDLINE AN 2000061195 in reciting that edotecarin is also used to treat neoplasia.

However, WO 95/15316 (abstract) discloses that edotecarin (title, abstract) is useful as an anti-tumor agent. In the absence of a showing of unexpected results commensurate in scope with the claims no unobviousness is seen in combining edotecarin and celecoxib to yield a kit containing each compound and use them in a

method to treat neoplasia. That is because each is taught by the art to be useful to treat the same condition.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims pending are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims allowed of U.S. Patent No. 6,649,645 and 5,972,986. Although the conflicting claims are not identical, they are not patentably distinct from each other because in the absence of a showing of unexpected results the comprising language of the instant method and the methods of '645 and '986 would render obvious the instant method of treating neoplasia using celecoxib and edotecaran.

Claims pending are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims pending of copending Applications No. 10/323065 and 11/022174. Although the conflicting claims are not identical, they are not patentably distinct from each other because in the

absence of an election of different compounds the methods of treating neoplasia of '065 and '174 would include the instant edotecaran and celecoxib.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant is requested to advise the Examiner of any other cases in which there may be obviousness-type double patenting.

IDS

Applicant is requested to confirm that the IDS' received August 14, 2003 and March 16, 2004 which cite John McKearn as the first named inventor are intended for the instant application for Jaime Masferrer.

The International Search Report was not considered since it is not a publication as defined in 37 CFR 1.98.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Cook whose telephone number is (571) 272-0571. The examiner can normally be reached on Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Renee Jones (571) 272-0547 in Customer Service.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The official fax number is 571-273-8300.

Rebecca Cook

Primary Examiner
Art Unit 1614

March 14, 2005